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TI Direct binding of a synthetic multichain polypeptide to class II major **histocompatibility** complex molecules on antigen-presenting cells and stimulation of a specific T-cell line require processing of the polypeptide
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AB T-cell activation involves the recognition of foreign antigens as a complex with self-major **histocompatibility** complex (MHC) proteins on the surface of antigen-presenting cells (APC). Protein antigens usually require uptake by the APC and processing that results in the generation of peptide fragments. The branched synthetic polypeptide (Tyr, Glu)-Ala--Lys was chosen as a model antigen to follow the processing requirements, leading to T-cell activation. It has been demonstrated, by using fixed APC and various inhibitors of proteases, that (Tyr,Glu)-Ala--Lys has to be processed to stimulate a (Tyr,Glu)-Ala--Lys-specific T-cell line of C3H.SW (H-2b) origin to proliferate. To det. whether processing of (Tyr,Glu)-Ala--Lys is required to allow its assocn. with the MHC class II mols., biotin was covalently attached to it. Binding of the biotinylated (Tyr,Glu)-Ala--Lys to MHC class II gene products on the surface of intact normal APC was directly detected by phycoerythrin-streptavidin. The specificity of the binding was confirmed by its inhibition with anti-I-Ab antibodies as well as with excess of nonlabeled (Tyr,Glu)-Ala--Lys. By introducing several inhibitors of proteases to the binding assay, it was substantiated that the proteolysis of (Tyr,Glu)-Ala--Lys is required to allow assocn. of the resulting peptidyl T-cell epitopes with the MHC class II mols. themselves. The presence of the biotin moiety in the resulting peptides suggests that the T-cell epitopes of (Tyr,Glu)-Ala--Lys contain the N-terminal portion of the side chains of the branched polypeptide. An apparent Kd of 8.05 .times. 10-8 M was detd., and optimal binding was detected after 10 h of incubation with the antigen. The latter phenomenon is not due to slow uptake, since uptake of (Tyr,Glu)-Ala--Lys occurs mainly during the first 30 min of incubation, but rather reflects the events of processing that precede MHC interaction.

BP, as followed by both cell proliferation and interleukin 2 secretion assays, were affected by Cop 1. For one line, a direct cross proliferation with Cop 1 was obsd., whereas in the other 7 lines and clones, Cop 1 specifically inhibited the responses to BP in a competitive dose-dependent manner. The inhibition of the response to BP is specific to Cop 1, as D-Cop 1 and another random acidic polymer, poly(Tyr,Glu,Ala) (TGA), both of which were previously demonstrated to be ineffective in suppression of exptl. allergic encephalomyelitis, did not inhibit the response to BP. Furthermore, Cop 1 specifically inhibited only the response to the T-cell lines and clones to BP. It did not inhibit their response to the mitogen Con A, nor did it inhibit the responses of the purified protein deriv.-specific T-cell line and clone. Cop 1 may be effective in suppression of exptl. allergic encephalomyelitis, not only because of the selective stimulation of suppressor T cells, as previously demonstrated, but also by specific inhibition of BP-specific effector T cells.